ADVANTAGES AND DISADVANTAGES OF CYSTATIN C FOR ASSESSMENT GLOMERULAR FILTRATION RATE

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ПРЕИМУЩЕСТВА И НЕДОСТАТКИ ЦИСТАТИНА С ДЛЯ ОЦЕНКИ СКОРОСТИ КЛУБОЧКОВОЙ ФИЛЬТРАЦИИ

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Assessing the rate of glomerular filtration is important in the diagnosis and prognosis of complications of kidney disease. Currently, creatinine is widely used in the assessment of glomerular filtration rate. However, creatinine is an imperfect biomarker because the amount of creatinine in a deposit depends on a person's age, gender, race, muscle size, and some medications they are taking. With this in mind, it is important to find the perfect biomarker and diagnose early kidney disease in determining and evaluating glomerular filtration rate. There are now excellent biomarkers in measuring glomerular filtration rate that have the ability to detect, predict, and diagnose disease at an early stage in a timely manner. One such biomarker is cystatin C. This article describes the determination of glomerular filtration rate by cystatin C, its advantages and disadvantages, and its application in clinical settings.

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Key words: *cystatin C, glomerular filtration rate, acute and chronic kidney disease, creatinine.*

Скорость клубочковой фильтрация является основным индикатором для диагностики и прогнозирования почечных болезней. В настоящее время скорость клубочковой фильтрации обычно определяют по уровню креатинина в крови. Однако креатинин в крови считается недельным биомаркером, повышенный уровень сывороточного креатинина может варьировать в широком диапазоне в зависимости от многих неренальных факторов (возраст, мышечная масса, пол, степень обезвоживания и др.). Поэтому для оценки скорости клубочковой фильтрация необходимо определять биомаркеры в реальном времени, что обеспечит раннюю диагностику и ускорит проведение эффективных профилактических и терапевтических мер. В настоящее время существуют перспективные биомаркеры, которые точно отражают скорость клубочковой фильтрации и позволяют в самые ранние сроки диагностировать патологию и своевременно начать лечебные и реабилитационные мероприятия по предупреждению развития хронической болезни почек. Этим требованиям в основном соответствует цистатин С. В статье описаны преимущества и недостатки этого метода, а также применение в клинических условиях.

Ключевые слова: *цистатин С, скорость клубочковой фильтрации, острая и хроническая болезнь почек, креатинин.*

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Introduction

Glomerular filtration rate (GFR) is considered one of the laboratory indicators that accurately indicate the activity of the kidneys and provide information about its physiology. Glomerular filtration rate has a wide range, depending on the pharmacological and pathological condition [1]. Basically, a decrease in GFR is considered one of the criteria for diagnosing acute and Chronic Kidney Diseases (CKD), and a wide range of applications to clinical action has been varied [2]. CKD weight levels are determined based on the amount of GFR. In addition, having GFR below 60 ml/min/1.73 m^2 for 3 months is the basis for pouring CKD diagnosis without other clinical signs [3]. The severity levels of CKD are shown in Table 1 below [4].

GFR determination was first proposed by the Danish scientist physiologist Paul Christian Brandt Reberg in 1926 [5]. In 1936, the therapist of the Soviet Union E.M. Tareev. He improved the determination of GFR and proposed the use of internal creatinine clearance, and therefore at the present time this technique is called the Reberga – Tareev test [6]. In a healthy person, the norm is gfr 120±25 ml/min/1.73 m^2.

Table 1. CKD levels

Levels		GFR quantity, ml/ min/1,73 м2
C1	high, optimal quantity	>90
C2	some decline	60-89
C3A	mid-level decline	45-59
C3Б	on a heavy level decline	30-44
C4	extrtmely heavy decline	15-29
C5	decline terminal level	15<

Modern medicine is conducting research on the way to finding simple, reliable and effective methods of grading GFR. Currently, there are several methods for determining GFR such as Cocroft – Golt (Cockcroft – Gault), MDRD (Modification of Diet in Renal Disease Study), Schwartz (Schwartz) for children [7]. All of the above styles determine Holda GFR based on creatine. Creatinine levels have been widely used in clinical settings for the last 50 years.

According to the results of numerous scientific works, the amount of creatinine is nonspecific in assessing the activity of nephrons [8]. Its amount is also counted depending on norenal factors (patient age, muscle size, race, gender and body water to the amount of salt, etc. [9] (fig. and the infusion therapies carried out affect the amount of creatinine in the blood [10].

It is known to us that some drugs (cimetidine, trimetoprim) reduce creatinine secretion and, as a result, there is an increase in the amount of transitor creatinine in the blood [11]. In addition, the production of creatinine in the blood can also vary. Various foods and muscle volume lead to significant fluctuations in creatinine levels in the blood [12]. On the other hand, low protein intake or cachexia can cause a decrease in creatinine levels [13].

It is found that 24-48 hours after structural and physiological changes in the ducts, an increase in the level of creatinine in the blood is increased [14]. Because the kidneys have a large functional reserve, so the amount of creatinine in the blood does not change until 50% of nephrons lose their working capacity [15]. It is difficult to assess the exact excretory function of the kidneys through the amount of creatinine.

There are several principles for assessing the performance of all nephrons through gfr. There are a number of treats that need to be dealt with additionally, even if their theoretical basis is well developed. Let's dwell on the Basic Rules.

- Choosing a suitable marker for a particular person in GFT identification.
- Marker without toxic properties
- Marker that separates from my organism only through the kidneys
- Free filter marker from ball blood vessels
- Reobsorbable and secretable marker
- Marker that does not bind to plasma proteins
- Marker not metabolized in the body
- Marker that does not enter cells and spreads freely outside cells

In addition, the marker must be determined through simple and reliable measurement techniques in biological fluids, harmless to the body.

In recent times, the relevance of the development of harmless, effective and modest methods of assessing GFT in clinical practice has increased even more. Given this, several exogenous markers are used in modern medicine. As an example," inulin, iohexol, DTPA-diethylentriamine pentaacetate acid " and others are widely used [16].

Inulin exogenous polysaccharide is considered to be the "gold standard" in determining GFT until now. However, due to its high cost, difficult solubility and too short a stay in the blood, it has not been widely used in clinical practice [17].

Iohexol is a low osmolality X-ray contrast agent it has been widely used in both clinical trials, but there are limitations in its application due to its allergenicity and nephrotoxicity [18].

DTPA diethylentriamine pentaacetate acid is used in the determination of GFR, but is little used in practice for its radioactive substance presence and nephrotoxic properties [19].

Another modern marker is cystatin C (Cys C), which has a molecular mass of 13.4 kda, a protein composed of 122 amino acids [20].

Cys C is an external inhibitor of cystatin proteases in the cell. Cys C monomer is in almost all body fluids

The way to prove the superiority of one style over another is considered to be the comparison of both styles with the ham "gold standard". But the rapid development of Medicine is also causing gold standards to change. But the introduction of new standards into clinical practice requires several dozen large scientific researches.

A number of studies have shown that serum Cys C levels diagnose GFR earlier and more accurately than creatinine [25]. And the evaluation of GFR through Cys C is also important and reliable in clinical practice from other calculation methods. Osama B. and according to other authors, in patients undergoing kidney transplantation, it is better to evaluate GFR with Cys C than in other methods with better binding (correlation) CCrCG, MDRD, CKD-EPI [26]. In addition, when checking GFR using Cys C, The Binding rate to dermographic pointers is lower than that of creatinine [27]. For example, the body muscle size and age binding rate of Cys C (R2 =0.01, P=0.803 and R2 =0.021, P=0.75) do not have statistical significance [28]. In contrast,

	 22-YR-OLD BLACK MAN	 53-YR-OLD WHITE MAN	 80-YR-OLD WHITE WOMAN
Serum creatinine	1,2 mg/dL	1,2 mg/dL	1,2 mg/dL
GFR as estimated by the MDRD equatoin	98 mL/min/1,73 m^2	66 mL/min/1,73 m^2	46 mL/min/1,73 m^2
Kidney function	Normal GFR or stage 1 CKD if kidney damage is also present	Stade 2 CKD if kidney damage is also present	Stage 3 CKD

Fig. 1. Low importance of creatinine in the diagnosis of renal calculi [13].

Table 2. Evaluation of GFR based on Cys C in blood plazma.

Equations	Authors
1. GFR (1,73/m 2) = -4,32+8,35/ Cys C	F.J. Hoek [2003]
2. GFR = 77,24 × Cys C –1,2623	A. Larsson. [2004]
3. GFR= 99,43 × Cys C –1,5837	
4. GFR (1,73 m 2) = 3,7+34,6/ Cys C	R.P. Woitas. [2000]
5. GFR= 124/ Cys C – 22,3	P. Sjostrom [2005]
6. GFR=86,49 × Cys C -1,686 × (0,948j)	A. Crubb [2005]
7. GFR =66,8 × Cys C –1,30	A.D.Rule [2006]
8. GFR=79,901 × Cys C –1,4389	M. Flodin [2007]
9. GFR=(100/ Cys C)-14	M. Tidman [2008]
10. GFR=127,7 × Cys C –1,17 × B3–0,13 (× 0,91j; × 1,06chk)	L.A. Stevens [2008]
11. GFR=177,6 × Cr – 0,65 × Cys C – 0,57 × B3 – 0,20(× 0,82j; × 1,11chk)	L.A. Stevens [2008]

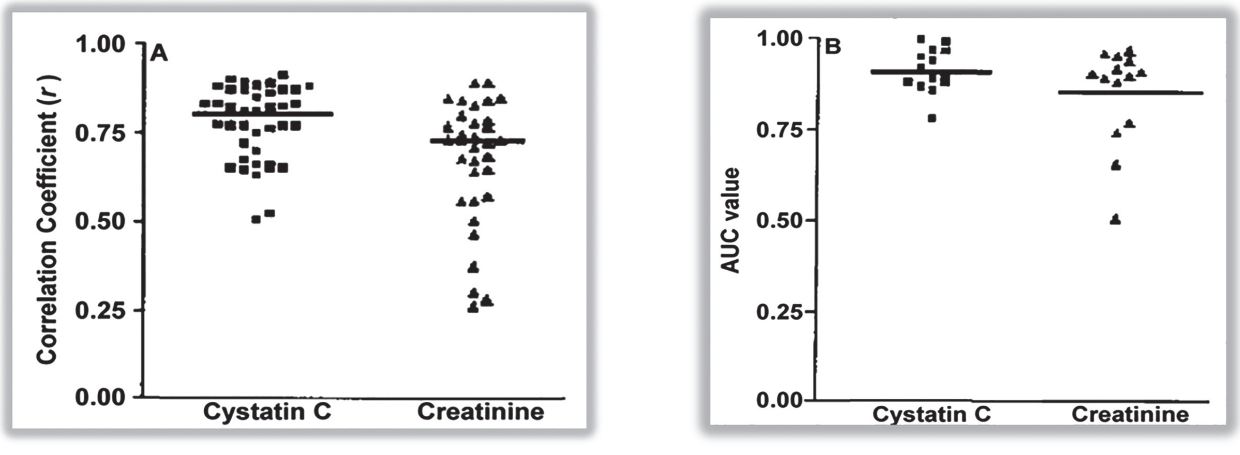

Fig. 2. Advantage of cyctatin C creatinine in determining the rate of glamerulyar filtration [29].

creatinine has a significant association with body muscle size and age (R2=0.54, P=0.001 and R2=0.47, P=0.001). As can be seen from the above data, the degree of dependence on individual pointers when checking Cys C GFR is low [29].

GFR ≤60ml/min/1,73m2 plasma Cys C content in diagnosis, has a higher 72% sensitivity and 64% compatibility (spesifichnost) than creatinine, and has a 0.92 (The area under the curve receiver operating characteristic (AUCROC) 95% reliability rate (ID 0.82-0.96), creatinine 66.2% sensitivity and 45.7% compatibility 0.83 ROC, ID (0,79-0,87) (p<0.001) [30].

On the other hand, the Cys C also has its own disadvantages. for example, Cys C analysis is 12 times more expensive than creatinine (3.0$ vs 0.25$) [31]. As we know, Clinical requires constant examination, even if there is no change in the function of the kidneys. This further increases clinical costs and causes restrictions on regular use in Cys C. In addition, Cys C analysis requires a highly specialized clinical laboratory and qualified staff [32].

According to the results of scientific research carried out at the latest, it is proposed to use Cys C and creatinine together in the early diagnosis of kidney pathology [33]. L.A. Inger, and according to other authors, when Cys C and creatinine were used together in diagnosing chronic kidney diseases in their competence, chronic kidney diseases were anicized in early boskich which reduced the mortality rate by 2.4 times [34]. In addition, the combined use of Cys C and creatinine in GFR determination showed 4 times better than in a separate application.

Conclusion

Creatinine is a laboratory marker that has been used for a long time to assess kidney activity and is considered a marker that has been used in diagnosis, forecasting and step-by-step treatment of patients. However, the amount of creatinine in the blood evaluates kidney activity late and depends on many norenal factors. Cys C is well studied and does not depend on body weight, gender, race, age, different from creatinine. In addition, Cys C is superior to bash biomarkers in that it can detect kidney diseases at a subclinical stage and predict CKDs in advance. On the other hand, the only drawback of the Cys C is relatively.

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GLOMERULYAR FILTRATSIYA TEZLIGINI BAHOLASH, SISTATIN C NING AHAMYATI VA KAMCHILIKLARI

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Buyrak kasalliklarini tashxislash va asoratlarini prognozlashda glomerulyar filtratsiya tezligini baholash muhim ahamyatga ega hisoblanadi. Hozirgi kunda glomerulyar filtratsiya tezligini baholashda asosan kreatinin miqdorini aniqlash usulidan foydalaniladi. Ammo kreatinin nomukammal biomarker hisoblanadi, chunki qondagi kreatinin miqdori inson yoshiga, jinsiga, irqiga, mushaklar hajmiga va ba'zi qabul qilayotgan dorilarga bog'liq. Shuni hisobga olib glomerulyar filtratsiya tezligini aniqlashda va baholashda mukammal biomarker topish va erta buyrak kasalliklarini tashxislash muhim sanaladi. Hozirgi vaqtda glomerulyar filtratsiya tezligini o'lchashda mukammal biomarkerlar mavjud bo'lib, ular o'z vaqtida buyraklar faoliyatini aniqlash, prognozlash va kasalliklarni erta darajasida tashxislash qobilyatiga ega. Xuddi shunday biomarkerlardan biri sistatin C hisoblanadi. Ushbu maqolamizda glomerulyar filtratsiya tezligini sistatin C orqali aniqlash, uning afzalliklari va kamchiliklari va klinik sharoitlarda qo'llash bayon etilgan.

Kalit so'zlar: *sistatin C, glomerulyar filtratsiya tezligi, o'tkir va surunkali buyrak kasalliklari (SBK), kreatinin.*

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